

Application ser. no. 10/782,698  
Attorney Docket No. W1107/20009  
Amendment Dated June 8, 2008

**REMARKS**

Claims 1-240, 243, 246-247, 251, 254-255 and 257-264 are canceled without prejudice.  
Claims 241-242, 244-245, 248-250, 252-253, 256, and 265- 316 are new. Claims 241-256 and 265-316 are pending.

**Amendment of the title of the application**

The change is intended to indicate that the claims focus on assays, rather than the fragments themselves.

**Retention of some of the language from Claim 110 in other claims**

Applicant has canceled elected independent Claim 110 (and claims 111-144 dependent on it) but retained much of its language through the various claim amendments.

Claim 110's reference back to Claim 1 is accounted for, in part, by incorporating some of the language from Claim 1 into Claim 249.

Claim 110's reference to Claim 3 is accounted for, in part, by incorporating some of the language from Claim 3 into a dependent claim, Claim 272.

Claim 110's reference to Claims 6 is accounted for, in part, by utilizing some of the language from Claims 110 and 6 in new independent Claim 276.

Claim 110's reference to Claims 9 and 11 is accounted, in part, by utilizing some of the language from Claims 110 and 9 and 11 in new independent Claim 289.

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Claim 110's reference to Claim 13 is accounted for, in part, by utilizing some of the language from Claims 110 and 13 new independent Claim 297.

### **Retention of some of the language of Claim 257 in other claims**

Applicant has canceled independent Claim 257 without prejudice but retained some of its language through the various claim amendments. Independent Claim 257 required that a fragment being assayed for comprise SEQ ID NO:1. The present amendment cancels Claim 257 (and its dependent claims) but adds new dependent Claims 281 and 294, which apply the SEQ ID NO:1 limitation to Claims 276 and 289, respectively.

### **Amendments to independent Claim 241**

This claim was amended to change "but less than 110 kDa" to "of a molecular weight of 140 kDa or less". Support for the change from "110 kDa" to "140 kDa" can be found the specification at page 16, lines 10-13, and Claim 110 as filed (given its dependence on Claim 1 as filed). Also, in the Remarks section of the Amendment of July 23, 2007 (at page 40) it is clear that the 140 kDa limit, not the 110 kDa limit, was intended for Claim 241.

This claim was also amended to include the phrase, "wherinc the size in kDa is that determined by gel electrophoresis after disulfide bond reduction" and thereby make it consistent with all the other independent claims where such kDa information is part of the claim.

The claim was also amended to include the phrase "such that the greater the plasma level of said thrombospondin fragment or fragments, the more likely that the diagnosis will be that a

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neoplastic disease is present in said individual". That phrase finds support in now-cancelled Claim 243, which was dependent on Claim 241, as well as the application generally.

### **Amendments to independent Claim 249**

In addition to incorporating some of the language from Claim 1 into Claim 249, the phrase, "and/or comprising an epitope therein" has been removed from Claim 249. New Claim 303 is an alternative way of describing the invention implied by "and/or comprising an epitope therein" that was in Claim 249.

The claim was also amended to include the phrase "such that the greater the plasma level of said thrombospondin fragment or fragments, the more likely that the diagnosis will be that a neoplastic disease is present in said individual". That phrase finds support in now-cancelled Claim 251, which is dependent on Claim 249, as well as the application generally.

### **New independent Claim 276**

Claim 276 incorporates some language from Claims 110 and 6.

The language "or is a portion thereof" from Claim 6 is replaced by "or is a portion of the range I-165 to Y-982, said portion being at least 150 amino acyl residues in size." The size of 150 amino acyl residues corresponds to the minimum size of the fragment in withdrawn Claim 6, which fragment extended from V-263 to K-412.

### **New independent Claim 289**

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Claim 289 incorporates some language from Claims 110 and Claims 9 and 11.

The phrase “purified and/or synthetic”, in Claims 9 and 11, is not included in Claim 289 because the phrase is irrelevant to an assay for plasma levels of fragments.

In Claim 289, the minimum molecular weight is 20 kDa, which is supported by the fact that the main gel fragments observed were in the range 20 to 140 kDa.

### **New independent Claim 297**

In addition to containing some language from Claims 110 and 13, new Claim 297 incorporates language from the paragraph starting at page 18, line 7 of the specification. In particular, the phrase, “heparin-binding sequence in the amino-terminal domain of thrombospondin” finds its origin at page 18, lines 17-18.

The phrase “purified and/or synthetic”, in Claim 13, is not included in Claim 297 because the phrase is irrelevant to an assay for plasma levels of fragments.

In Claim 297, the minimum molecular weight is 20 kDa, which is supported by the fact that the main gel fragments observed were in the range 20 to 140 kDa.

### **New independent Claim 303**

New Claim 303 is an alternative way of describing the invention implied by “and/or comprising an epitope therein” that was in Claim 249 but has now been removed from it.

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### **New independent Claim 309**

New independent Claim 309 finds support in the specification at page 8, lines 18-27 and page 18, lines 7-13.

### **Dependent claims**

Dependent Claims 242 and 250 now contain the phrase, “such that the greater the extent to which the first individual’s plasma fragment level exceeds the second individual’s plasma level, the more likely that the diagnosis will be that a neoplastic disease is present in the first individual“, formerly in now cancelled Claims 243 and 251.

New dependent Claims 277- 280 and 290-293, have language similar to that of dependent claims 242, 244-245 and 248 as they appeared prior to this Amendment.

New dependent Claims 298-300 and 304-306, have language similar to that of dependent claims 242, 244, and 248 as they appeared prior to this Amendment.

New dependent Claims 281 and 294 are based on language in Claim 257 as it appeared prior to this Amendment.

New dependent claims 265-267 and 282–284 define the minimum molecular weight of the fragments (or portions in the case of Claims 282-284) as 20 kDa, which is supported by the fact that the main gel fragments observed were in the range 20 to 140 kDa.

New dependent claims 268-271, 285-288, 295-296, 301-302, 307-308, and 316 either limit the binding agent to being an antibody or limit one or both binding agents to being an antibody, all of which limitations are supported at many places in the specification (See for

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example, discussion of “Binding agents”, pages 15-16.).

### **Objection to the specification (Paragraph 3 of the Office Action)**

The Examiner has objected to the presence of browser-executable code in the application. These have been removed by the amendments to the specification.

### **Objection to Claims 230 and 251 (Paragraph 4 of the Office Action)**

These claims were objected to because “person” was misspelled as “persion”. Claims 230 and 251 have been cancelled and therefore the spelling was not corrected.

### **Rejection of Claims 110-144, 162, 228-233 and 241-264 under 35 U.S.C. 112, second paragraph (Paragraph 6 of the Office Action)**

These claims have been rejected on the grounds that four independent Claims 110, 228, 241, 249, and 257 and four related dependent claims 111, 229, 242, 250 and 258, are not clear as to how one of ordinary skill makes use of the diagnostic results. Claims 110, 111, 228, 229, 257 and 258 have been canceled.

Claims 241 and 249 have been amended to include the language, “such that the greater the plasma level of said thrombospondin fragment or fragments, the more likely that the diagnosis will be that a neoplastic disease is present in said individual”. Similar language has been included in new independent Claims 276, 289, 297, 303 and 308.

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Claims 242 and 250 have been amended to include the language, “such that the greater the extent to which the first individual’s plasma fragment level exceeds the second individual’s plasma level, the more likely that the diagnosis will be that a neoplastic disease is present in the first individual”. Similar language has been included in new dependent Claims 277, 290, 298, and 304.

**Provisional rejections of Claims 110-144, 162, 228-233 and 241-264 on the grounds of nonstatutory obviousness (Paragraphs 8 and 9)**

Applicant believes that a response to this rejection would be premature at this time considering the ongoing nature of the prosecution of the two application with ser. nos. 10/419,462 and 10/525,610, respectively, as well as the ongoing nature of the present application.

**McCarthy et al. reference cited in parallel application Ser. No. 10/419,462**

McCarthy et al., US application publication No. 20030166017 was cited in the Office Action of 3-25-08 in parallel application 10/419,462 as the basis of a rejection under 35 USC §102.

Applicant believes that the claims in present application ser. no. 10/782,968, which have steps correlating fragment levels with diagnosis and also have language making it clear that the claims related to neoplastic diseases, would overcome an anticipation rejection based on

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McCarthy et al, which relates to cardiovascular diseases.

Applicant had a telephonic interview with the Examiner on April 24, 2008, in parallel application ser. no. 10/419,462. A summary of the call will appear in Applicant's response to the most recent Office Action in that case. Applicant appreciated the call and found it very useful in formulating the above comments regarding McCarthy et al.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for initial examination and allowance, the Examiner is invited to phone Applicants' undersigned attorney at **610-724-2952**.

Respectfully submitted,

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